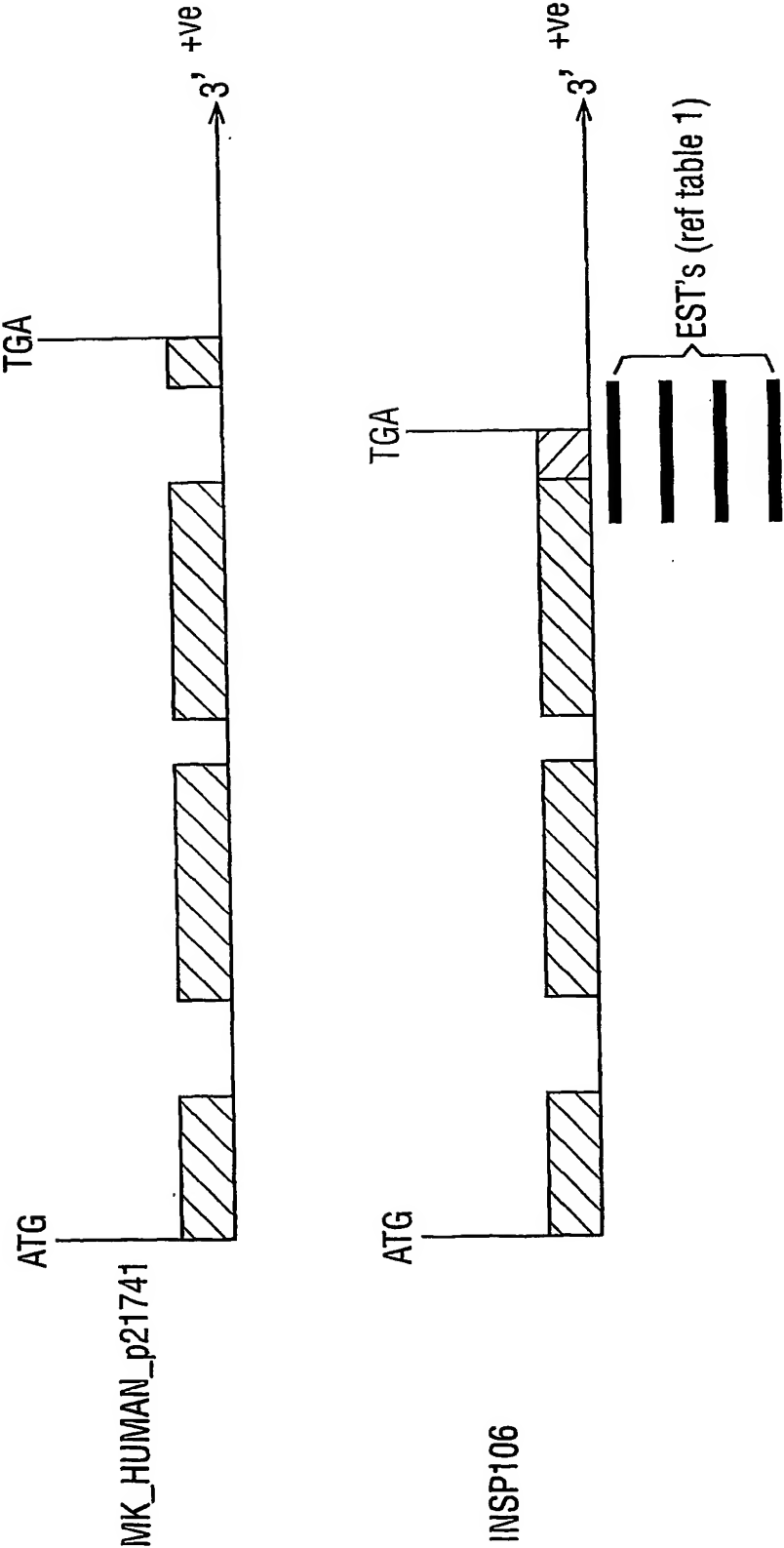


FIG. 1



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FIG. 2(CONTD.)

→	swaUP2174PMK_HUMAN	60	KDCGNGIF	70	TCGAQTQRI	80	TCGAQTQRI	90	VPCKNV	100	DFGADC	110	NWGAACDGGTGT	V
→	swlclul		KDCGVGTF		TCGAQTQRI		TCGAQTQRI		VPCKNV		DFGADC		NWGAACDGGTGT	V
	swaUPQ9RDE9/Q9RDE6		KDCGVGTF		TCGAQTQRI		TCGAQTQRI		VPCKNV		DFGADC		TWGAACDGGTGT	A
	swaUP1202PMK_MOUSE		KDCGMGTF		TCGAQTQRI		TCGAQTQRI		VPCKNV		DFGADC		SWGAACDGGTGT	A
	swaUPQ9R1S9/Q9R1S9		KDCGMGTF		TCGAQTQRI		TCGAQTQRI		VPCKNV		DFGADC		SWGAACDGGTGT	A
	swaUP2402PMK_CHICK		KDCGLGYT		TCGDEK		TCGDEK		VPCKNV		KFGADC		SWGGCSAKTGV	T
	swaUP48330PTA1_XENLA		KDCGAGT		TCXET		TCXET		VPCKNV		DFGADC		SWGHCNAT	T
	swaUP48331PTA2_XENLA		KDCGAGT		TCXET		TCXET		VPCKNV		DFGADC		SWGHCNAT	T
	swaUPQ9W768/Q9W768		GDCGNGI		TCNEOT		TCNEOT		VPCKNV		DFGADC		SWGHCNAT	T
	swaUPQ9DDG2/Q9DDG2		GDCGNGI		TCNEOT		TCNEOT		VPCKNV		DFGADC		SWGHCNAT	T
	swaUPQ9W767/Q9W767		GDCGNGI		TCNEOT		TCNEOT		VPCKNV		DFGADC		SWGHCNAT	T
	swaUP19281P79281		GDCGQGM		TCNEOT		TCNEOT		VPCKNV		DFGADC		SWGHCNAT	T
	swaUP21782PTN_BOVIN		GDCGLGT		TCNEOT		TCNEOT		VPCKNV		DFGADC		SWGHCNAT	T
	swaUP21246PTN_HUMAN		GDCGLGT		TCNEOT		TCNEOT		VPCKNV		DFGADC		SWGHCNAT	T
	swaUP20035PTN_MOUSE		GDCGLGT		TCNEOT		TCNEOT		VPCKNV		DFGADC		SWGHCNAT	T
	swaUPQ9CSX8/Q9CSX6		GDCGLGT		TCNEOT		TCNEOT		VPCKNV		DFGADC		SWGHCNAT	T
	swaUPQ9CYE3/Q9CYE5		GDCGLGT		TCNEOT		TCNEOT		VPCKNV		DFGADC		SWGHCNAT	T
	swaUP48332PTB1_XENLA		GDCGLGT		TCNEOT		TCNEOT		VPCKNV		DFGADC		SWGHCNAT	T
	swaUP48333PTB2_XENLA		GDCGLGT		TCNEOT		TCNEOT		VPCKNV		DFGADC		SWGHCNAT	T

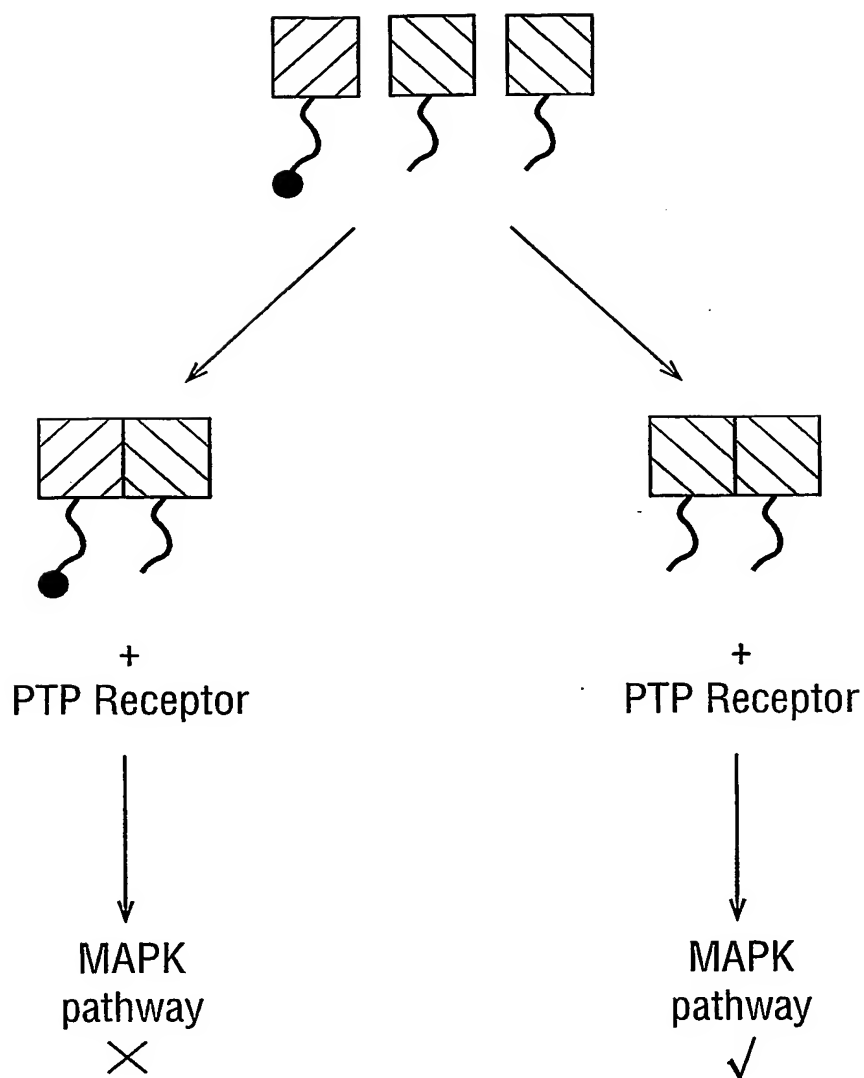
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FIG. 2(CONTD.)



→ swaUP21741MK_HUMAN	QGTLL	ARVNAQCQETLRVT	PCTPKT	AAKAK	GGKD	---	170
→ swlchr11	QGTLL	ARVNAQCQETLRVT	PCTPKT	AAKQORKE	GGVGLSRGAAPPRL	---	160
swaUPQ9W0E9Q9W0E6	QGTLL	ARVNAQCQETLRVT	PCS PKT	AAKAK	GKED	---	150
swaUP12025MK_MOUSE	QGTLL	ARVNAQCQETLRVT	PCTSKT	TKAK	GKD	---	140
swaUPQ9R1S9Q9R1S9	QGTLL	ARVNAQCQETLRVT	PCTSKT	AAKAK	GKD	---	130
swaUP24052MK_CHICK	SGTLL	ALVNAECLEVVYVX	PCTAKM	AAKAK	GKD	---	120
swaUP48330PTA1_XENLA	SGTLL	ALVNAECQQTVEAT	PCS LKT	SKGX	GKE	---	110
swaUP48331PTA2_XENLA	SGTLL	ALVNAECQQTVEAA	PCS LKT	SKGX	GKE	---	100
swaUPQ9W768Q9W768	SGTLL	ALFNAECQTTIKVX	PCTPKT	PKGGEKK	GKEN	---	90
swaUPQ9D0G2Q9D0G2	SGTLL	ALFNAECQTTIKVX	PCTPKT	PKGGEKK	GKEN	---	80
swaUPQ9W767Q9W767	TGSL	ALFMVHCQQTVISVT	PCTTKV	PKG	GKGN	---	70
swaUP79281PT9281	TGSL	ALHNAECQKTVTIS	PCGKVT	PQAESKK	EGKKQEKMLD	---	60
swaUP21782PTN_BOVIN	TGSL	ALHNAECQKTVTIS	PCGKLT	PQAESKK	EGKKQEKMLD	---	50
swaUP21246PTN_HUMAN	TGSL	ALHNAECQKTVTIS	PCGKLT	PQAESKK	EGKKQEKMLD	---	40
swaUP20935PTN_MOUSE	TGSL	ALHNAECQKTVTIS	PCGKLT	PQAESKK	EGKKQEKMLD	---	30
swaUPQ9CSX6Q9CSX6	TGSL	ALHNAECQKTVTIS	PCGKLT	PQAESKK	EGKKQ	---	20
swaUPQ9CYE5Q9CYE5	TGSL	ALHNAECQKTVTIS	PCGKLT	PQG	KKLSF	---	10
swaUP48332PTB1_XENLA	SGSL	ALHNAECQKTVTIS	PCGKVT	LQE-SKK	EGKNXEXLLD	---	0
swaUP48333PTB2_XENLA	NGSL	ALHNAECQKTVTIS	PCGKVT	LQE-SKK	EGKNXEXLLD	---	

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FIG. 3



KEY

 Midkine monomer with lysine rich C-terminal tail INSP106 with modified C-terminal

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FIG. 4

	10	20	30	40	50	60
swall	MQHRGFLLLTLLALLALTS	SAVAKKKDKVKKGGPGSECAE	WAWG	CTPSSKDCG	VGFREGT	
chr11_	MQHRGFLLLTLLALLALTS	SAVAKKKDKVKKGGPGSECAE	WAWG	CTPSSKDCG	VGFREGT	
	10	20	30	40	50	60
	70	80	90	100	110	120
swall	CGAQTQRI	RCRVPCNWKKEFGADCKYKFEN	WGACDGGTGT	KVRQGT	LKKARYNAQCQETI	
chr11_	CGAQTQRI	RCRVPCNWKKEFGADCKYKFEN	WGACDGGTGT	KVRQGT	LKKARYNAQCQETI	
	70	80	90	100	110	120
	130	140				
swall	RVTKPCTP	KTAKAKA-KKGKG	-----	KD		
chr11_	RVTKPCTP	KTAKAKAQ	RKEKGVGLSRGA	APPPRL		
	130	140	150			

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FIG. 5

1 cgggtgcgtcc gggctagcgg cgagggggccg ccccaagtct tcccaccgcc gccaccttag
 61 cagcccgaact tggggcctgg aaagtggagc acgcggaggt gggagggccc tgcacgcggc
 121 ccccgtggg gaaggggacg ggccagggat tcagactcgg gctctcccct caggatgcag
m q

 181 caccgaggct tcctcctcct caccctcctc gccctgctgg cgctcacctc cgcggtcggc
h r g f l l l t l l a l l a l t s a v a
→
INSP10A-F1
 241 aaaaagaaag ataaggtgaa gaagggcggc ccggggagcg agtgcgctga gtgggcctgg
k k k d k v k k g g p g s e c a e w a w
 301 gggccctgca ccccagcag caaggattgc ggcgtgggtt tccgcgaggg cacctgcggg
g p c t p s s k d c g v g f r e g t c g
 361 gccagaccc agcgcateccg gtgcagggtg ccctgcaact ggaagaagga gtttgagacc
a q t q r i r c r v p c n w k k e f g a
 421 gactgcaagt acaagtttga gaactgggtt gcgtgtgatg ggggcacagg caccaaagtc
d c k y k f e n w g a c d g g t g t k v
 481 cgccaaggca ccctgaagaa ggcgcgtac aatgctcagt gccaggagac catccgcgtc
r q g t l k k a r y n a q c q e t i r v
 541 accaagccct gcaccccaa gaccaaagca aaggccaaag gtcagcgaaa ggagaagggg
t k p c t p k t k a k a k g q r k e k g
 601 gtggggctgt cgcggggggc tgccccccc ccccccgcc tgtgagggga caattccaag
v g l s r g a a p p p p r l
 661 ttaaacctta agttttgagt cctggccagt ggcttcctga catgcctca ctggtctcc
←
INSP10A-R1
 721 ctgcctggaa aagtctgaag atgggcaact caagagaggc cgcaggtgat gctggggaca
 781 taaatcctcc ctggcccaa tagggaccaa ctcaaactac tccattggag catctggctt
 841 aggac

Position and sense of PCR primers →
In italics: predicted signal peptide

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FIG. 7

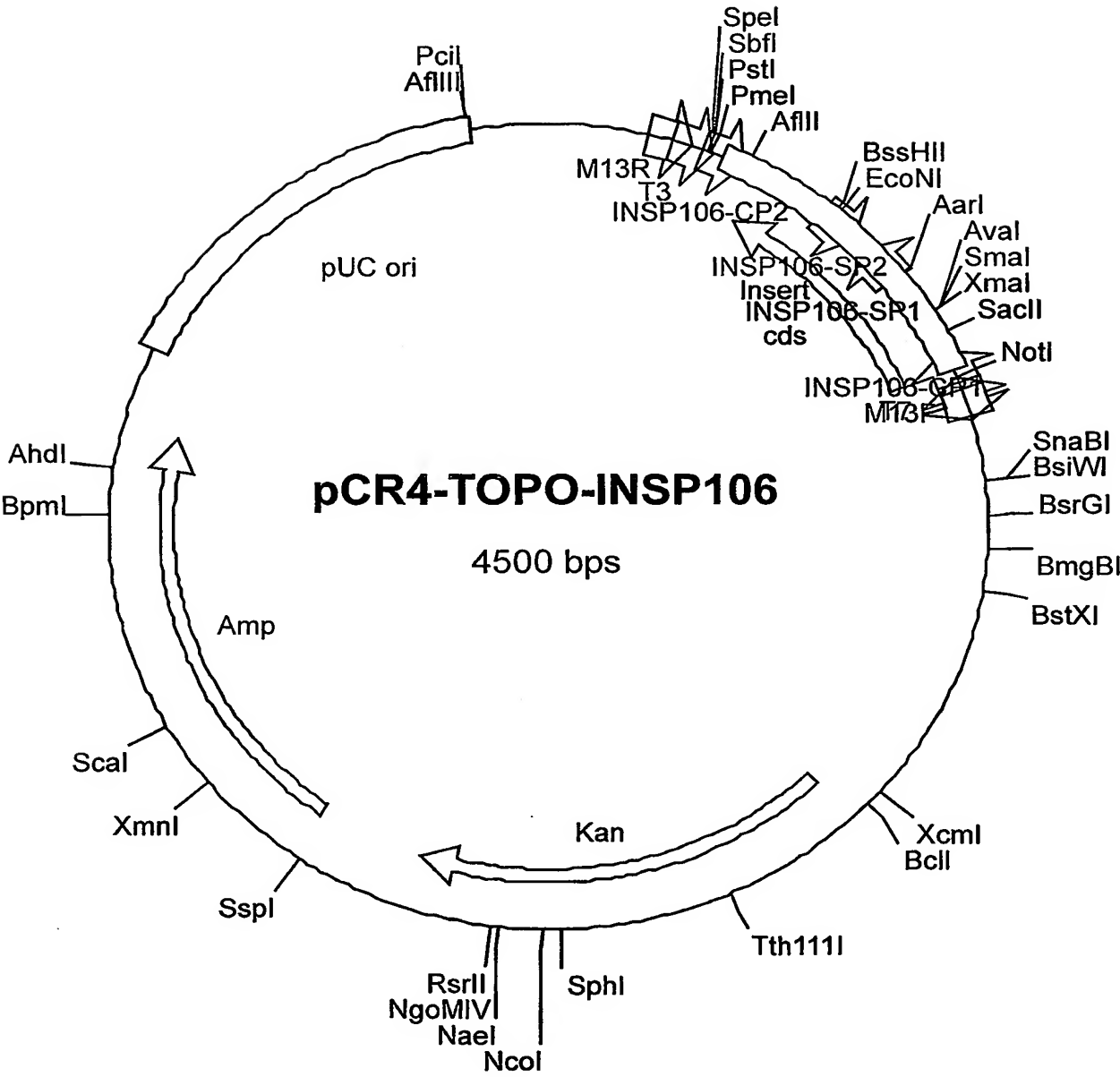
Map of pCR4-TOPO-INSP106

Molecule: pCR4-TOPO-INSP106, 4500 bps DNA Circular

Type	Start	End	Name	Description
MARKER	205		M13R	M13 rev priming site
MARKER	243		T3	T3 priming site
MARKER	295		INSP106-CP2	INSP106-CP2 primer site
MARKER	522		INSP106-SP2	INSP106-SP2 sequencing primer site
MARKER	616		C INSP106-SP1	INSP106-SP1 sequencing primer site
GENE	833	366	C cds	INSP106 cds
MARKER	837		C INSP106-CP1	INSP106-CP1 primer site
REGION	837	295	C Insert	INSP106-CP1/-CP2 PCR product
MARKER	890		C T7	T7 priming site
MARKER	898		M13F	M13 for priming site
GENE	1702	2496	Kan	Kanamycin resistance gene ORF
GENE	2700	3560	Amp	Ampicillin resistance gene ORF
REGION	3705	4378	pUC ori	pUC origin

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FIG. 7(contd)



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FIG. 8

Map of pDONR 221

Molecule: pDONR221, 4759 bps DNA Circular
File Name: pDONR221.cm5

Description:

Type	Start	End	Name	Description
REGION	295	268	C rrnB T2	transcription termination sequence
REGION	470	427	C rrnB T1	transcription termination sequence
REGION	536	553	21M13	M13 Forward primer
REGION	570	801	attP1	
GENE	1197	1502	ccdB	
GENE	1844	2503	Cm r	Chloramphenicol resistance gene
REGION	2751	2982	attP2	
REGION	3040	3023	C M13 Rev	M13 Reverse primer
GENE	3153	3962	Kan r	
REGION	4083	4756	pUC ori	

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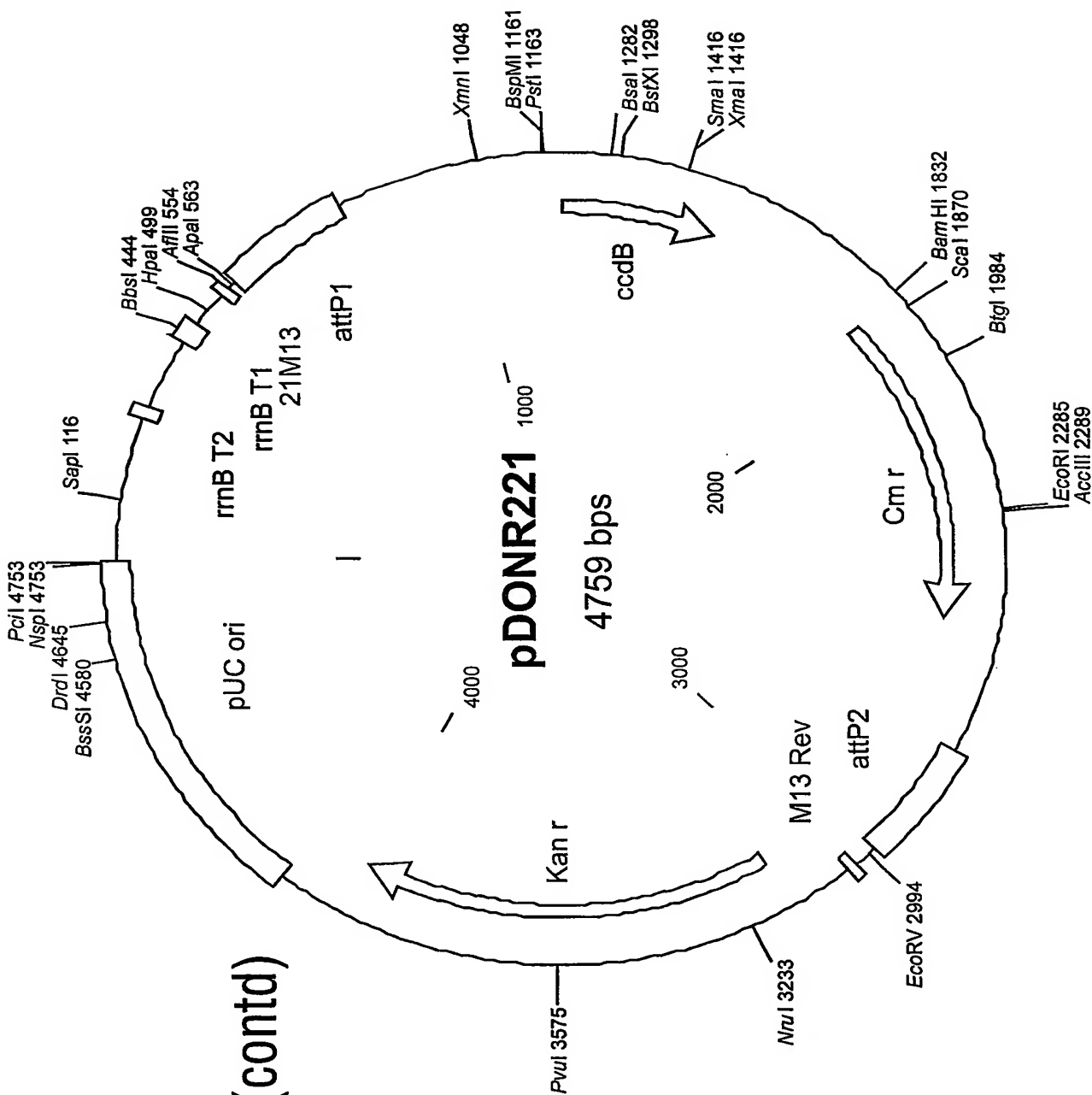


FIG. 8(contd)

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FIG. 9

Map of expression vector pEAK12d

Molecule: pEAK12 d, 8760 bps DNA Circular
 File Name: pEAK12DEST.cm5

Description: Mammalian cell expression vector (plasmid ID 11345)

Molecule Features:

Type	Start	End	Name	Description
REGION	2	595		pmb-ori
GENE	596	1519	Amp	
REGION	1690	2795	EF-1alpha	
REGION	2703	2722		position of pEAK12F primer
REGION	2796	2845		MCS
MARKER	2855		attR1	
GENE	3256	3915	CmR	
GENE	4257	4562	ccdB	
MARKER	4603		C attR2	
REGION	4733	4733		MCS
REGION	4734	5162		poly A/splice
REGION	4819	4848	C	position of pEAK12R primer
GENE	5781	5163	C PUR	PUROMYCIN
REGION	6005	5782	C tK	tK promoter
REGION	6500	6006	C Ori P	
GENE	8552	6500	C EBNA-1	
REGION	8553	8752	sv40	

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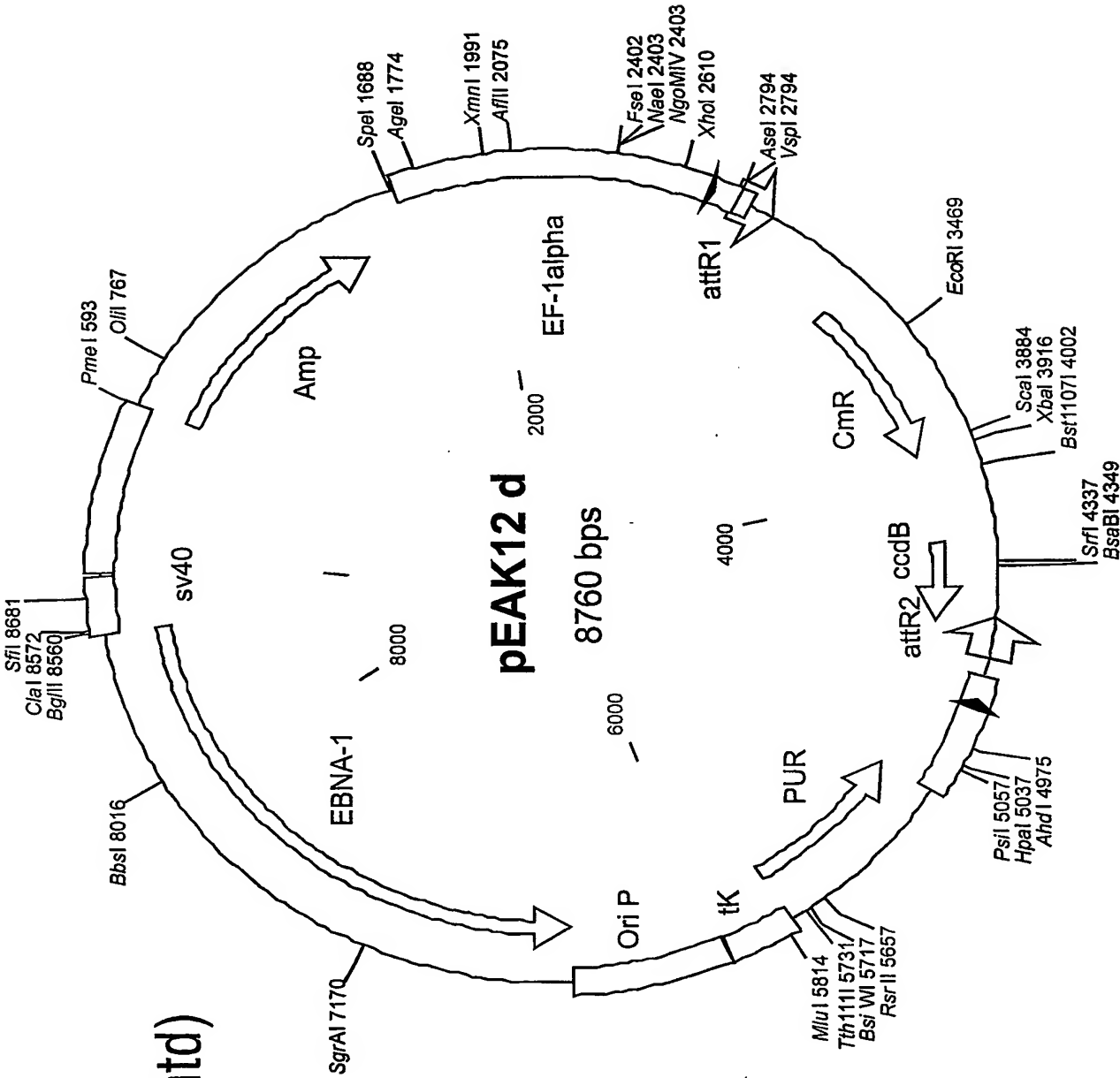


FIG. 9(contd)

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FIG. 10

Map of Expression vector pDEST12.2

Molecule: pDEST 12.2, 7278 bps DNA Circular
 File Name: pDEST12-2.cm5

Description: Eukaryotic expression vector

Type	Start	End	Name	Description
REGION	15	608	CMV	CMV promoter
MARKER	648		M13R	M13R primer
REGION	687	706	SP6	SP6 promoter
REGION	730	854	attR1	
GENE	963	1622	Cm	
GENE	1964	2269	ccdB	
REGION	2310	2434	attR2	
GENE	2484	2464	C T7	T7 promoter
MARKER	2512		C 21M13	21M13 primer
REGION	2784	3050	pA	SV40 polyadenylation signal
REGION	3176	3631	f1	f1 intergenic region
REGION	3791	4099	P SV40	SV40 ori & early promoter
GENE	4158	4952	Neo	
REGION	5016	5064	pA	synthetic poly adenylation signal
GENE	5475	6335	Amp	
REGION	6480	7153	ori	pUC ori

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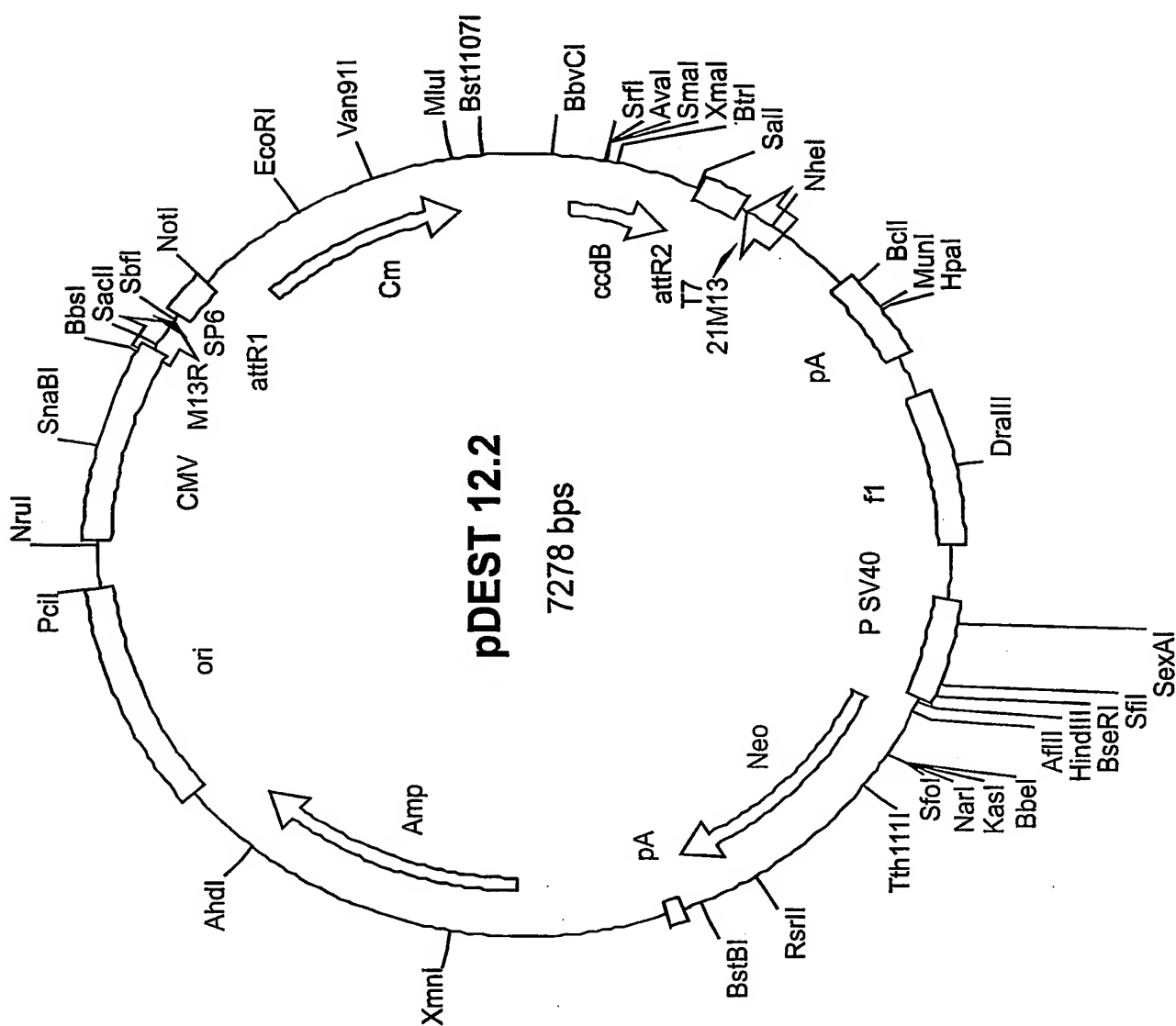


FIG. 10(contd)

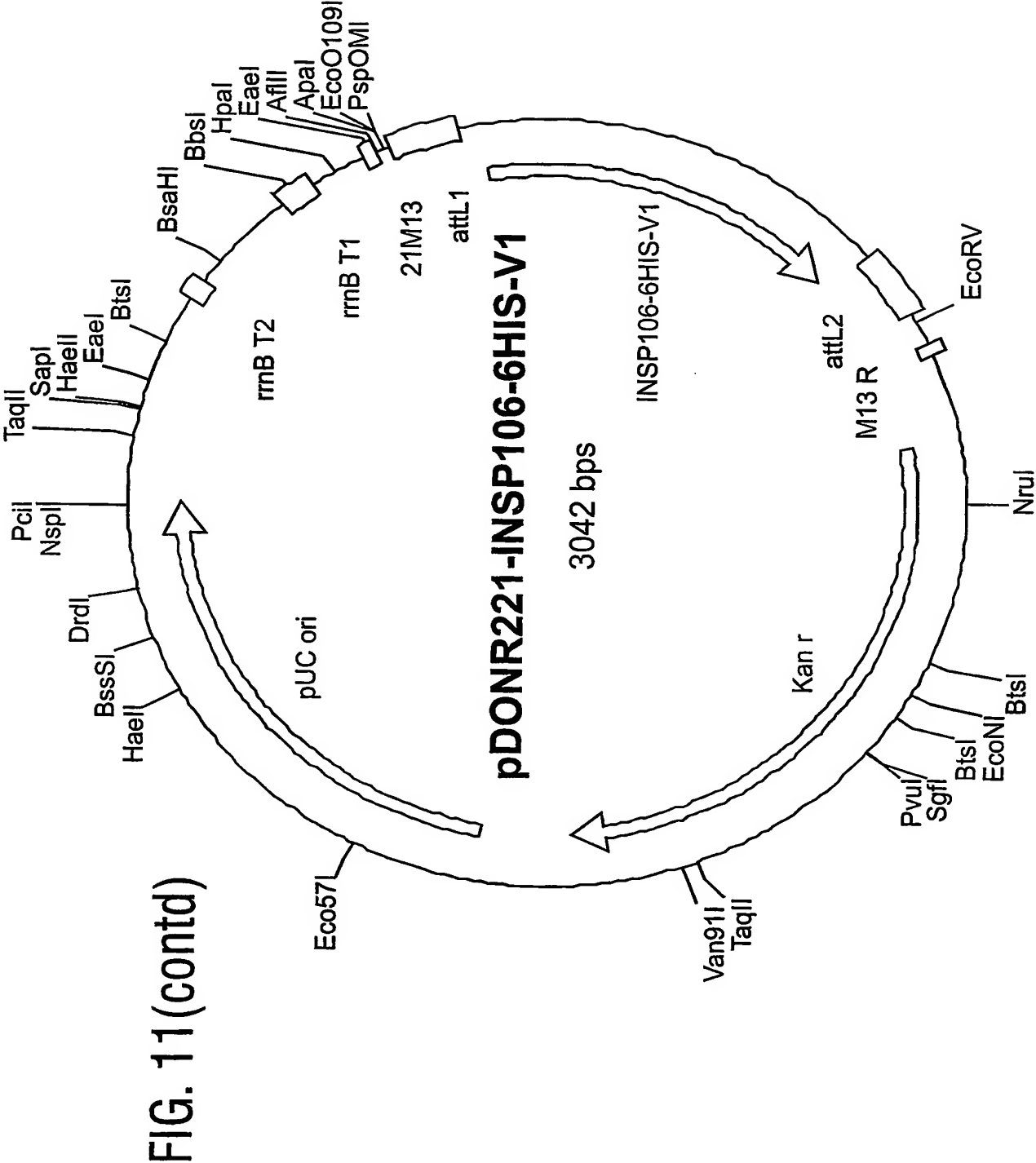
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FIG. 11

Map of pDONR221-INSP106-6HIS

Molecule: pDONR221-INSP106-6HIS-V1, 3042 bps DNA Circular

Type	Start	End	Name	Description
REGION	295	268	C rrnB T2	transcription termination sequence
REGION	470	427	C rrnB T1	transcription termination sequence
REGION	536	553	21M13	21M13 primer
REGION	570	651	attL1	
GENE	677	1162	INSP106-6HIS-V1	
REGION	1177	1265	attL2	
REGION	1323	1307	C M13 R	M13R primer
GENE	1436	2245	Kan r	
GENE	2366	3039	pUC ori	



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FIG. 12

Map of pEAK12d-INSP106-6HIS

Molecule: pEAK12d-INSP106-6HIS-V1, 7435 bps DNA Circular

Type	Start	End	Name	Description
REGION	2	595	pmb-ori	
GENE	596	1519	Amp	
REGION	1690	2795	EF-1alpha	
REGION	2796	2845	MCS''	
REGION	2855	2874	attB1	
GENE	2888	3373	INSP106-6HIS-V1	
REGION	3381	3402	attB2	
REGION	3408	3408	'MCS	
REGION	3409	3837	'A	poly A/splice
GENE	4456	3838	C PUR	PUROMYCIN
REGION	4680	4457	C tK	tK promoter
REGION	5175	4681	C Ori P	
GENE	7227	5175	C EBNA-1	
REGION	7228	7427	sv40	

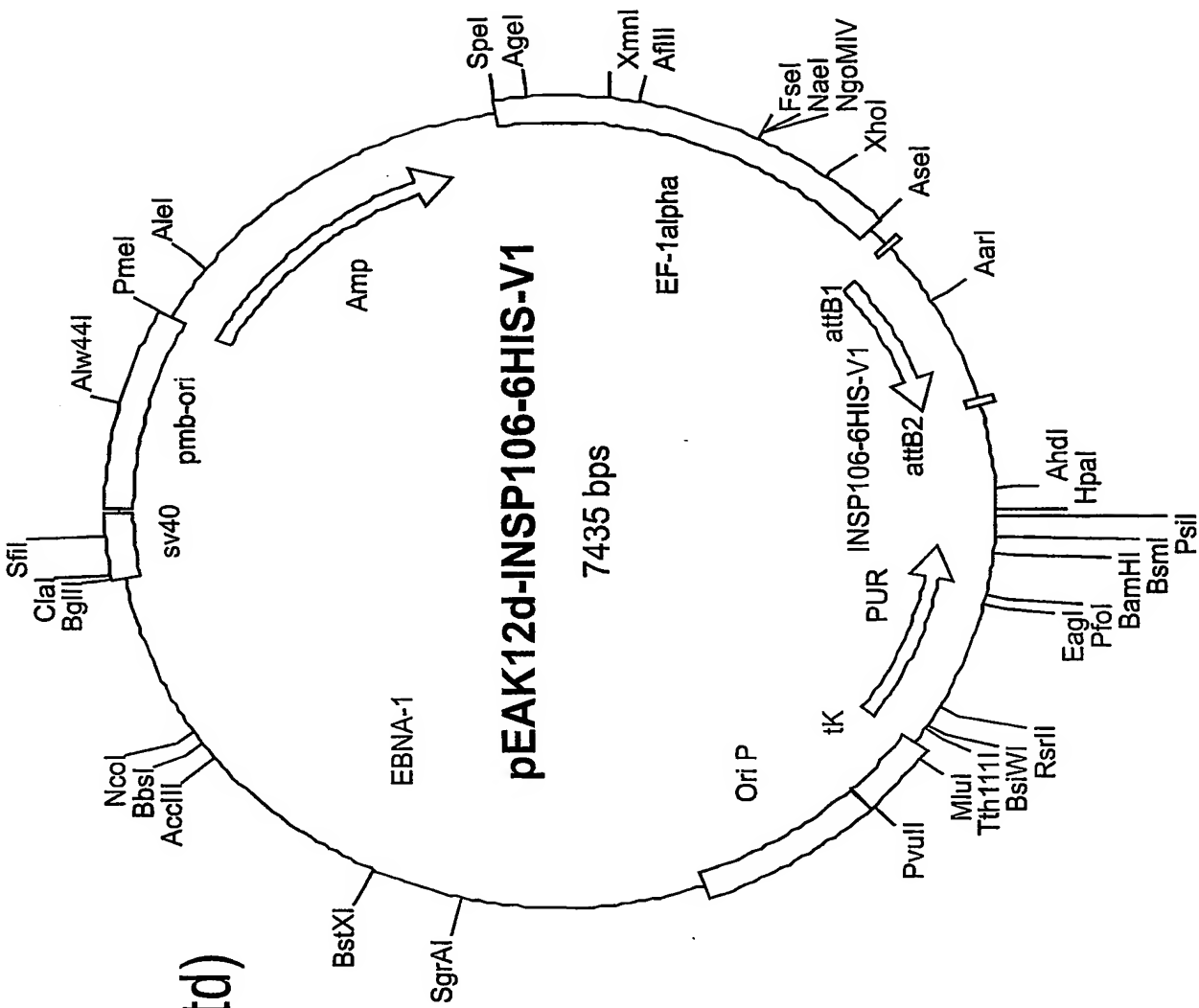


FIG. 12(contd)

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FIG. 13

Map of pDEST12.2-INSP106-6HIS

Molecule: pDEST12.2-INSP106-6HIS-V1, 6121 bps DNA Circular

Type	Start	End	Name	Description
GENE	15	537	CMV promoter	
REGION	648	665	M13rev	M13R primer
REGION	687	704	SP6	SP6 primer
REGION	730	762	attB1	
GENE	763	1248	INSP106-6HIS-V1	
REGION	1252	1277	attB2	
REGION	1327	1307	C T7	T7 promoter
REGION	1356	1338	C 21M13	21M13 primer
GENE	1462	1824	pA	SV40 polyadenylation signal
GENE	2018	2474	f1	f1 intergenic region
GENE	2538	2956	P SV40	SV40 ori & early promoter
GENE	3001	3795	Neo	
GENE	3859	3907	pA	poly adenylation signal
GENE	4318	5178	Amp	
GENE	5327	5966	ori	pUC ori

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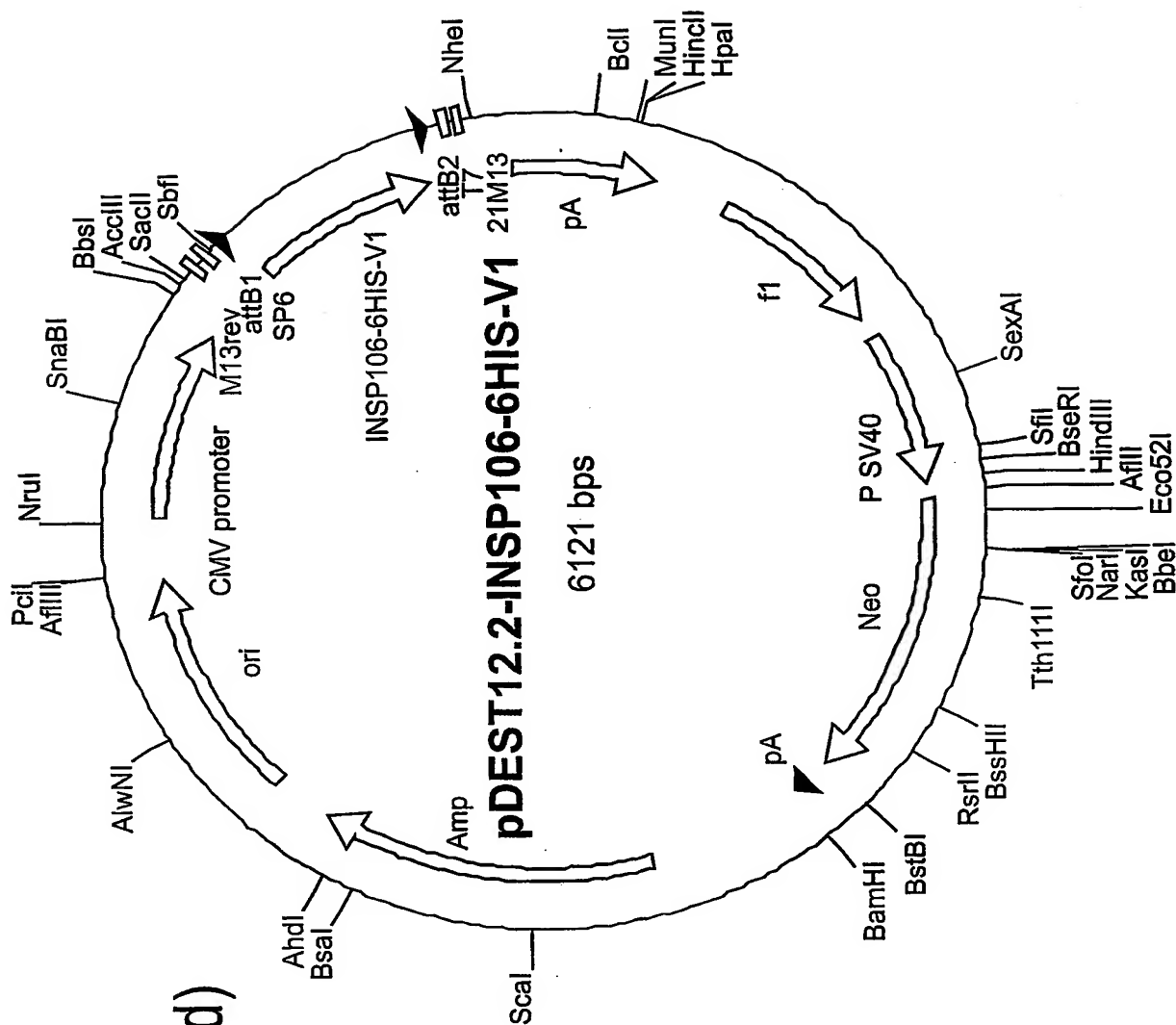


FIG. 13(contd)